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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,563	12/12/2003	Joseph A. Sorge	25436/2345C	2401

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
02/28/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/734,563	SORGE ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *11 and 22-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment of claims 1-7, in the paper of 9/30/2007, is acknowledged. Claims 1-26 are still at issue and are present for examination. Claims 1-22 are still at issue and are present for examination.

Applicants' arguments filed on 9/30/2007, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Applicant's previous election with traverse of Group I, Claims 1-10 and 12-21 in the paper of 10/23/2006, is acknowledged as well as applicants traversal in the paper submitted on 9/30/2007.

Applicants submit that Applicant's response to the restriction requirement filed 23 October 2006 ("Response") specifically pointed out the reasons why the restriction requirement was improper. As noted in the Response, each of the SEQ ID Nose. 83-108 recited in the pending claims represents the sequence of a related DNA polymerase, including a high level of amino acid sequence homology to the Family B class of polymerases.

Applicants submit that by requiring Applicant to elect a single species of mutant DNA polymerase the Office has improperly limited the scope of the claims through its requirement for restriction. Specifically, in issuing the restriction requirement, the Office has, without Applicant's permission or approval, limited the scope of the pending claims to a specific species disclosed in the specification (mutant versions of SEQ ID NO:89).

Applicant respectfully submits that it has a statutory right under 35 U.S.C. § 112, second paragraph, to claim the subject matter it regards as their invention as it chooses. Issuing a restriction requirement by incorporating an unclaimed limitation in an effort to limit the claim to disclosed embodiments, with the idea that Applicant would have to carve up that claim and pursue the non-elected subject matter in separate applications, violates this right under § 112. Indeed, the C.C.P.A. has characterized such action as tantamount to a refusal to examine. *See In re Weber,* 198 U.S.P.Q. 328 (C.C.P.A. 1978); *In re Haas,* 198 USPQ 334 (C.C.P.A. 1978).

In view of the above remarks, Applicant requests the Office to reconsider and withdraw the restriction requirement as to each of the mutant Archaeal DNA polymerases covered by the pending claims. In the event that the Office does not withdraw the restriction requirement, Applicant reserves the right to Petition the Commissioner to withdraw the restriction requirement, and/or to prosecute the non-elected claims in divisional or continuation applications.

Applicant's complete traversal continues to be acknowledged, however, is found nonpersuasive for the reasons previously made of record and repeated herein. Even though by applicant's submission SEQ ID NOs: 83-108 are highly related, it continues that these are structurally different DNA polymerase molecules and thus properly restricted. Applicant's submission that the Office has improperly limited the scope of the claims through its requirement for restriction is not found persuasive on the basis that applicant is not prevented from claiming applicant's invention more broadly such that

each of the referenced SEQ ID NOs: are encompassed by applicant's claims. Thus applicant's traversal is not found persuasive and the restriction requirement remains.

Claims 11 and 22-26 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 and 12-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office action as it applied to Claims 1-10 and 12-21. In response to this rejection applicants have amended claims 1-7 and traverse the rejection as it applies to the newly amended claims.

Applicants submit that the specification discloses several mutant DNA polymerases having different mutations at V93 as well as several working examples using different Archael DNA polymerases.

Applicants submit that in order to meet the written description requirement, applicants need only describe the claimed invention in a manner such that one of skill in

the art would understand that at the time of filing, applicant was in possession of the invention as claimed. Applicants submit that applicants have met this initial requirement, in that applicant's specification provides the sequences for a range of archaeal DNA polymerases showing where to mutate to achieve the desired reduction in base analog detection activity. Applicants point out that they disclose many different archael DNA polymerases and the corresponding nucleotide sequences. Applicants further submit that given the sequence similarities of the disclosed polymerases, it is reasonable to expect that mutations corresponding to the V93 mutations shown would have similar effects in other archael DNA polymerases. Applicants thus submit that applicants were in possession of more than simply the V93 mutants of SEQ ID NO: 89 described in the specification.

Applicant's complete argument is acknowledged, however not found persuasive for the reasons previously stated and repeated herein. As previously stated, claims 1-10 and 12-21 are directed to all possible archael DNA polymerases and compositions and kits comprising said archael DNA polymerase, wherein said mutant is a Pfu DNA polymerase (SEQ ID NO: 89) and further comprising at least one amino acid mutation in an exoI , exoII, or exoIII motif and another amino acid mutation at position V93 of the polymerase, wherein said polymerase is deficient in 3'-5' exonuclease activity. While it is acknowledged that applicants provide additional mutations of the disclosed polymerases that are deficient in 3'-5' exonuclease activity, these additional referred to mutants are not sufficient to adequately describe the claimed genus of any archael DNA polymerase deficient in 3'-5' exonuclease activity, wherein said mutant comprises at

least one amino acid mutation in an exoI , exoII, or exoIII motif and another mutation at position V93 of the polymerase. While applicants have provided additional archael DNA polymerase sequences, as well as additional mutants of SEQ ID NO: 89, deficient in 3'-5' exonuclease activity, applicants have not adequately described the claimed genus of any archael DNA polymerase deficient in 3'-5' exonuclease activity, wherein said mutant comprises a mutation in a exoI , exoII, or exoIII motif and at least one mutation at position V93 of the polymerase.

Applicants argument that the disclosed species of archael DNA polymerases and the disclosed mutants of SEQ ID NO: 89 are sufficient to provide a particular structure to function/activity relationship that would put one in possession of the genus of all possible mutant archael DNA polymerases with a reduced base analog detection activity comparing a mutation in a exoI , exoII, or exoIII motif and having a mutation corresponding to V93 is not persuasive. As previously stated, the specification fails to describe additional representative species of these mutant DNA polymerases by any identifying structural characteristics or properties other than the activities recited in the claims, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-10 and 12-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a Pfu DNA polymerase comprising the amino acid sequence of SEQ ID NO: 89 with a single amino acid substitution at position V93, does not reasonably provide enablement for any possible archael DNA polymerases and compositions and kits comprising said archael DNA polymerase, wherein said mutant is a Pfu DNA polymerase (SEQ ID NO: 89) further comprising at least one amino acid mutation in an exoI, exo II or exo III motif and another amino acid mutation at position V93 of the polymerase, wherein said polymerase is deficient in 3'-5' exonuclease activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was stated in the previous office action as it applied to Claims 1-10 and 12-21. In response to this rejection applicants have amended claims 1-7 and traverse the rejection as it applies to the newly amended claims.

Applicants submit that applicants specification coupled with the knowledge in the art provides substantial guidance as to the specific, conserved motifs within Archael DNA polymerases that are associated with the 3'-5' exonuclease activity of the polymerase. Applicants submit those domains associated with such activity and that

contrary to the previous office action, applicant's specification in combination with the art provides a known correlation between structure and function.

Applicants submit that the other Wands factors also weigh in favor of enablement. Applicants submit that the level of skill in the art was high, and applicant's specification discloses several working examples. Applicants further submit that applicants provide detailed information on site-directed mutagenesis necessary to generate the necessary mutants.

Applicant's complete argument is acknowledged, however not found persuasive for the reasons previously presented and repeated herein. It continues that while methods to produce specific variants (i.e. exo I, exoII, exoIII and mutants of V93) of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., deficient in 3'-5' exonuclease activity) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of mutant archael polymerases would have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. For example applicants state in their specification that encompassed by "archael" DNA polymerases are both the Family B/pol I-type group or the pol II group, yet it appears that applicants arguments are predominantly in support of the Family B/pol II group.

While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable

amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting deficiencies in 3'-5' exonuclease activity; (B) the general tolerance of Archael Family B/pol I-type and pol II-type DNA polymerases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of any Archael DNA polymerase including both Family B/pol I-type and pol II-type DNA polymerases with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to reduce the base analog detection activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those mutant archael DNA polymerases of the claimed genus having the claimed activities.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any mutant archael DNA polymerase with a reduced base analog detection activity. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24

(CCPA 1970)). Without sufficient guidance, determination of those mutant archael DNA polymerases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10 and 12-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-5, 13, 15, 17-29, 31-42, 58-66 of copending Application No. 10/298,680. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims of both applications are drawn to an Archael DNA polymerase comprising

an amino acid sequence of SEQ ID NO: 89, further comprising at least one amino acid mutation in an exoI, II, or III motif and another mutation at V93, wherein said DNA polymerase is deficient in 3'-5' exonuclease activity.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants request that this provisional rejection be held in abeyance until that time in which one of the two patent applications in question is deemed in condition for allowance, Is acknowledged.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rgh
2/19/2008

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652